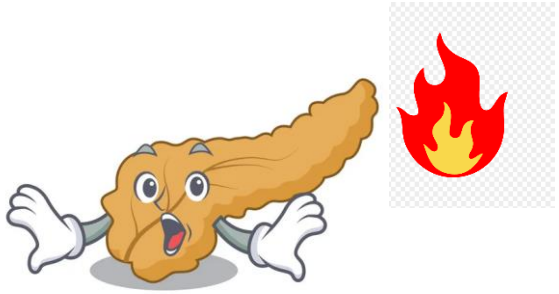

Burning Issues in Pancreatic Pain:
Risk Predictions: Pancreatic Pain

Melena Bellin MD

Professor, Pediatrics and Surgery

University of Minnesota Medical Center & Masonic Children's Hospital

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Disclosures

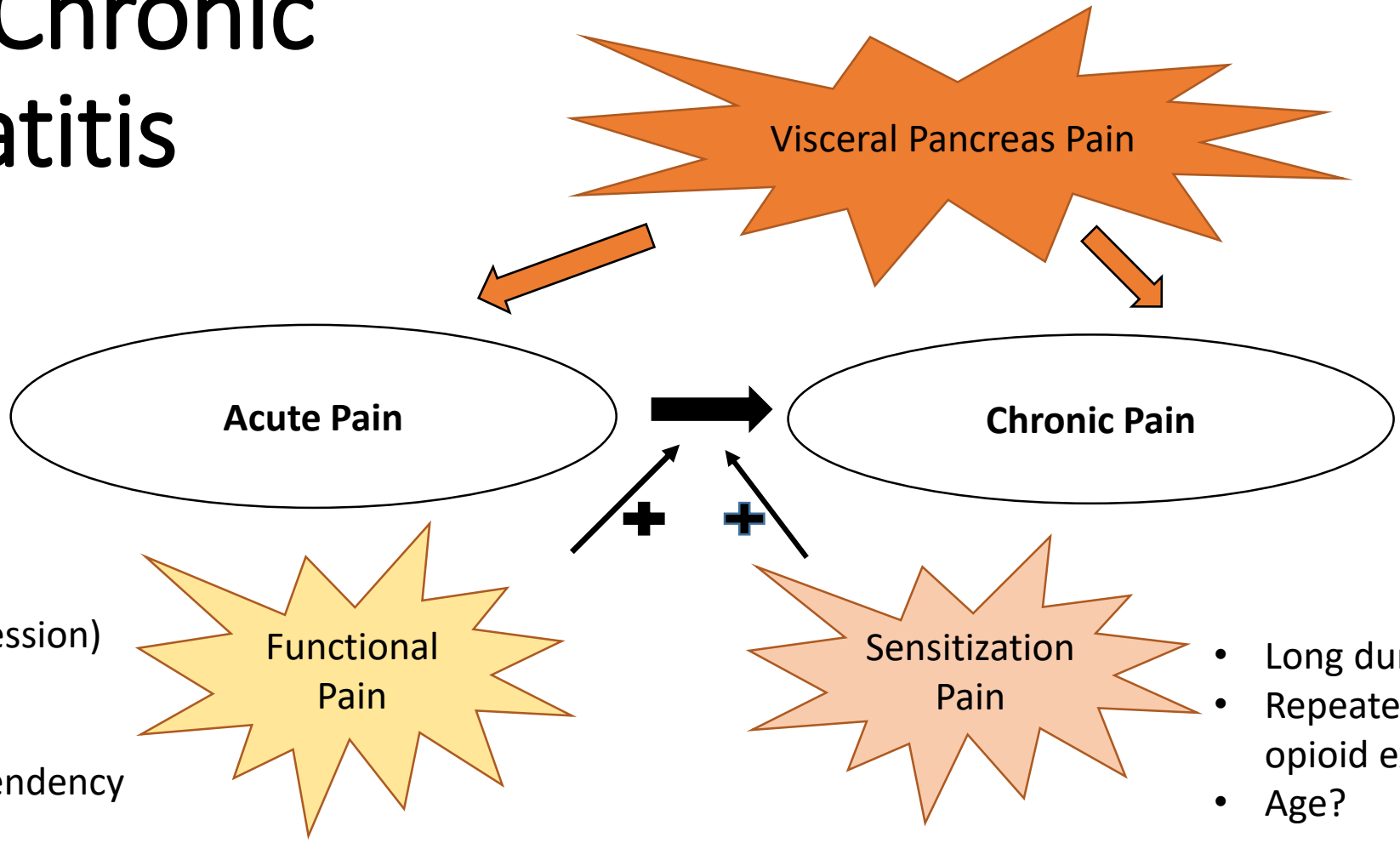
- Research Support:
  - Viacyte
  - Dexcom
- Insulet- DSMB membership
- Ariel Precision Medicine- Advisory Board

Risk Factors for Pancreas Pain

- Chronic pancreatitis is a heterogeneous disease
  - Variable disease course, including pain burden
  - Variable response to treatment
- What factors may contribute to high pain burden?
- What predicts response to treatment?
  - Pain relief vs persistent pain

Multi-Factorial Pain in Chronic Pancreatitis

- Disease cause
- Disease interventions/treatments
- Age



- Mental health (anxiety/depression)
- Social support structure
- Chemical dependency

- Long duration of pain
- Repeated /prolonged opioid exposure
- Age?

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TPIAT Procedure

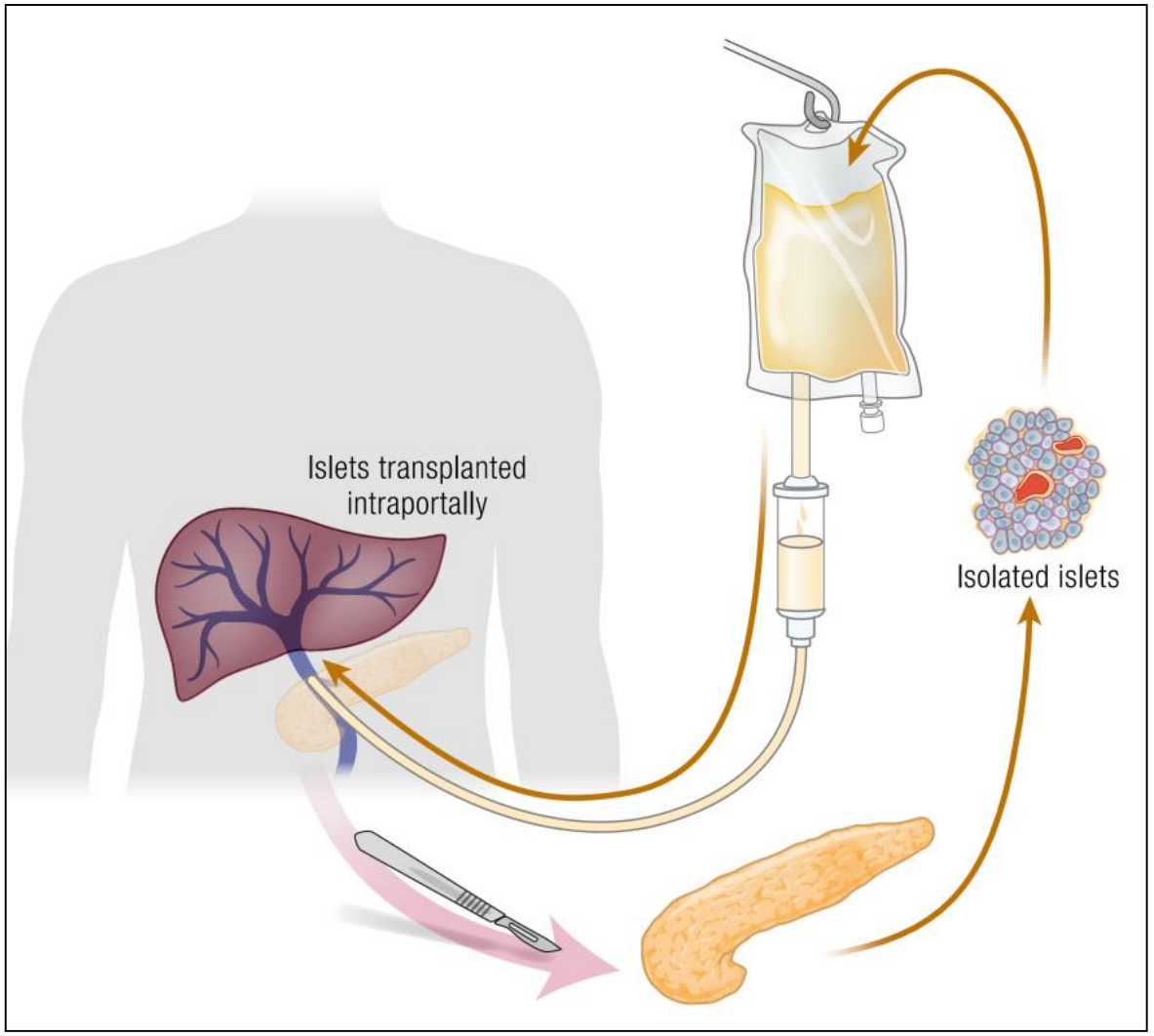

Figure from Endo Rev 40(2):631

1) **Pancreatectomy** (and associated GI and biliary anastomoses)
   - **Goal**= relieve pain

2) **Islet isolation and islet autotransplant**
   - **Goal=** minimize diabetes

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Factors Predicting Outcomes After a Total Pancreatectomy and Islet Autotransplantation Lessons Learned From Over 500 Cases

Srinath Chinnakotla, MD,† Gregory J. Beilman, MD,* Ty B. Dunn, MD, MS,* Melena D. Bellin, MD,†‡ Martin L. Freeman, MD,§ David M. Radosevich, RN, PhD,* Mustafa Arain, MD,§ Stuart K. Amateau, MD, PhD,§ J. Shawn Mallery, MD,§ Sarah J. Schwarzenberg, MD,† Alfred Clavel, MD,¶ Joshua Wilhelm, MS,‡ R. Paul Robertson, MD,§ Louise Berry, RN,* Marie Cook, MPH,† Bernhard J. Hering, MD,*‡ David E. R. Sutherland, MD, PhD,*‡ and Timothy L. Pruett, MD**

- **Associated with persistent 'pancreatitis' pain:**
  - Pancreas Divisum
  - Whipple
  - Repeated ERCP stents
  - BMI >30 kg/m2
  - **Opioid use >5 years pre-TPIAT**

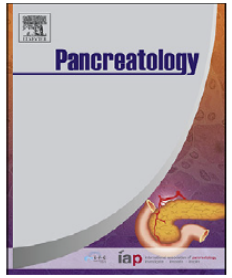
Response to TPIAT

Pancreatology 20 (2020) 762–771

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan



The role of total pancreatectomy with islet autotransplantation in the treatment of chronic pancreatitis: A report from the International Consensus Guidelines in chronic pancreatitis

Maisam Abu-El-Haija [a, b], Takayuki Anazawa [c], Gregory J. Beilman [d], Marc G. Besselink [e], Marco Del Chiaro [f], Ihsan Ekin Demir [g], Ashley R. Dennison [h], Vikas Dudeja [i], Martin L. Freeman [j], Helmut Friess [g], Thilo Hackert [k], Jorg Kleeff [l], Johanna Laukkarinen [m], Marlon F. Levy [n], Jaimie D. Nathan [o], Jens Werner [p], John A. Windsor [q], John P. Neoptolemos [r], Andrea R.G. Sheel [s], Tooru Shimosegawa [t], David C. Whitcomb [u], Melena D. Bellin [d, v, *]

[a] Division of Pediatric Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
[b] Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
[c] Division of Hepato-Biliary-Pancreatic Surgery and Transplantation, Department of Surgery, Graduate School of Medicine, Kyoto University, Japan
[d] Department of Surgery, University of Minnesota Medical Center, Minneapolis, MN, USA
[e] Department of Surgery, Amsterdam Gastroenterology and Metabolism, Amsterdam UMC, University of Amsterdam, the Netherlands
[f] Department of Surgery, University of Colorado Anschutz Medical Campus, Denver, CO, USA
[g] Department of Surgery, Klinikum Rechts der Isar, School of Medicine, Technical University of Munich, Munich, Germany

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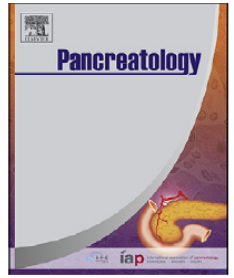


Table 3

Potential risk factors for worse pain or poor diabetes mellitus outcomes after TPIAT, bas

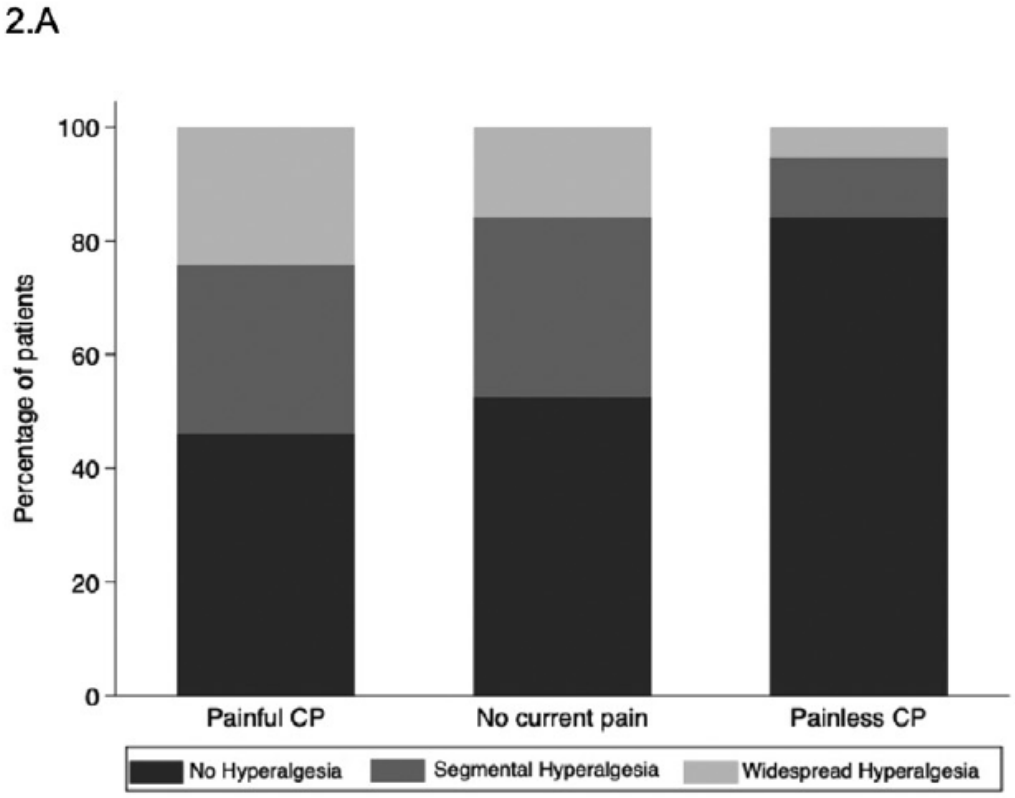
Risk Factors Persistent Pain, Opioid Dependence, or Poor Quality of Life
• Pancreas divisum
• Obesity (BMI >30 kg/m2)
• Previous pancreatic surgery (Whipple)
• Previous endoscopy and the number of endoscopic stents
• Older age
• High amount of preoperative narcotic intake
• Alcoholic pancreatitis

Potential outcome predictors (POST preliminary data, ~250 participants)

- Opioid use decreased [~1/4th on opioids at 1 year]
  - Age and opioid use pre-TPIAT associated w/1 year opioid use
  - Longer duration of disease was a risk factor in children (rarely on opioids at 1 year)
- SF-12 PCS increased ≥5 points in most
  - But in adults, smoking and anxiety associated with lower PCS

Preliminary unpublished data from POST

Sensitization is associated with higher pain burden, and may be more prevalent in alcohol-related CP



- Higher rates of hyperalgesia by QST with painful CP, or intermittent painful CP.
- Trend towards higher proportion of alcoholic disease in sensitization groups (~50% vs 34% in no hyperalgesia, p=0.09)

Clinical Gastroenterology and Hepatology 2022;20:153–161

In other pancreatic surgeries, pre-operative QST was associated with risk for persistent pain

Altered central pain processing after pancreatic surgery for chronic pancreatitis

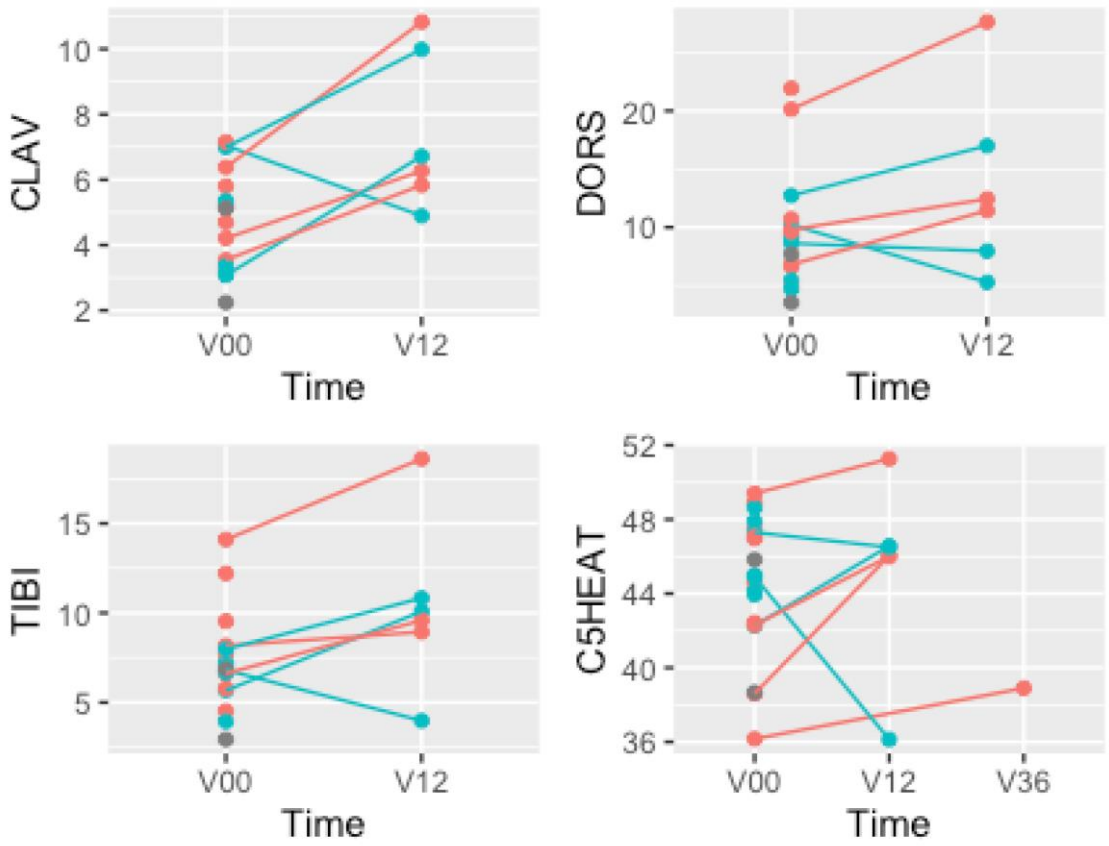
S. A. Bouwense[1], U. Ahmed Ali[3], R. P. ten Broek[1], Y. Issa[4], C. H. van Eijck[5], O. H. Wilder-Smith[2] and H. van Goor[1]

	Good pain outcome	Poor pain outcome	*P**
ePDT (mA)			
Sum of dermatomes	11·2 (10·0–12·3)	7·1 (4·7–9·5)	0·008
Dermatome C5	5·2 (3·9–6·4)	3·4 (2·6–4·7)	0·039
Dermatome L4	5·9 (4·7–7·3)	3·2 (2·3–5·1)	0·003
ePTT (mA)			
Sum of dermatomes	13·1 (11·5–18·0)	11·3 (6·9–14·5)	0·051
Dermatome C5	6·9 (5·3–8·6)	4·8 (4·2–7·4)	0·028
Dermatome L4	6·5 (5·7–8·0)	4·6 (3·4–6·6)	0·079
CPM			
Latency (s)	113 (42–180)	40 (25–180)	0·316
Response (%)	21·3 (−5·8 to 37·1)	−12·1 (−40·1 to 21·1)	0·021

British Journal of Surgery 2013; **100**: 1797–1804

QST and response to TPIAT

- Small cohort of 20 patients pre-TPIAT
- QST Pre-TPIAT
  - Pressure and heat stimuli
  - Ice bucket conditioning (CPM)
- Trend towards higher pain thresholds for heat and pressure after surgery but unclear relationship to opioid use



Opioid use at 6 months, Y=teal, N=pink

Unpublished data from POST

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Disease etiology and risk for persistent pain

Hereditary (PRSS1)

TABLE 1. Demographic Characteristics and 1-Year Outcomes for 64 Patients With *PRSS1* Undergoing TPIAT

1-yr outcomes	
Not using opioids, n (%)	48 (of 57 with data) (85)
Average daily pain score (n = 34), mean (SD)	1.47 (1.74)
SF-36: MCS (n = 37), mean (SD)	49.6 (9.9)
SF-36: PCS (n = 37), mean (SD)	52.2 (9.1)
Insulin independent, n (%)	18 (28.1)
Graft failure, n (%)	10 (15.6)
Hemoglobin A1c level (%), mean (SD)	6.87 (1.55)
Fasting glucose, mean (SD), mg/dL	119 (45)
Fasting C-peptide, mean (SD), ng/mL	0.86 (0.52)
Stimulated C-peptide, mean (SD), ng/mL	2.30 (1.38)

More likely to use opioids with increasing age and disease duration, but only 15% opioid requiring at 1 year overall

(*Pancreas* 2018;47: 466–470)

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(*Pancreas* 2018;47: 466–470)

Alcoholic

Table 5. Short Form-36: Patients with Alcoholic Pancreatitis Undergoing Islet Cell Autotransplantation

	Survey				
Description	**Preoperative**	**6 mo**	**1 y**	**2+ y**	**p Value**
Physical functioning	34.7	35	34.9	32.8	0.98
Role physical	32.3	32.1	30.7	31.2	0.99
Bodily pain	31	40.3	37.7	34.3	<0.01
General health	32.4	37	29.1	30	0.33
Vitality	38.5	42.9	34	38.2	0.27
Social functioning	35.2	34.7	31.3	28.3	0.49
Role emotional	30.6	26.4	23.5	24.7	0.72
Mental health	38.2	32.7	28.5	31.4	0.25
Physical component	31.1	41.1	36	36.2	0.10
Mental component	37.5	31.6	26	28.8	0.20

No improvement in McGill pain score.
EtOH disease was associated with worse pain outcomes.

(J Am Coll Surg 2013;216:591–598.

Conclusions

- Predictors for response to treatments remain poorly defined but may include:
  - Sensitization (QST measures)
  - Age and disease duration
  - Opioid exposure pre-treatment
  - Mental health comorbidities
  - Alcohol use history or smoking
  - Disease causes (genetic vs idiopathic vs alcoholic)
- Some of these risk factors may impact ongoing chronic pain through sensitization and functional pathways
- Better defining patient /disease risks and novel biomarkers or measures will help target major procedures (surgeries/TPIAT) to the ‘right’ candidates

Acknowledgements

NIDDK | NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

The National Pancreas Foundation

American Diabetes Association.

CDMRP Department of Defense Peer Reviewed Medical Research Program

POST TPIAT Team

Clinical research group

Melena Bellin, bell0130@umn.edu

University of Minnesota
Masonic Children's Hospital